

098 22 MAR 2001

RECEPTOR BASED ANTAGONISTS AND METHODS OF MAKING AND USING

claims priority of International application No. PCT/US99/22049, filed on September 22, 1999, which

5 This application claims priority of U.S. Application No. 08/313,942 filed May 19, 1999, which claims priority of U.S. Provisional Application No. 60/111,858 filed September 25, 1998. Throughout this application various publications are referenced. The disclosures of these publications in their entireties are hereby incorporated by reference into this application.

1

BACKGROUND OF THE INVENTION

Although discovered for varying biological activities, ciliary neurotrophic factor (CNTF), leukemia inhibitory factor (LIF), oncostatin M (OSM) and
15 interleukin-6 (IL-6) comprise a defined family of cytokines (referred to herein as the "CNTF family" of cytokines). These cytokines are grouped together because of their distant structural similarities [Bazan, J. Neuron 7: 197-205 (1991); Rose and Bruce, Proc. Natl. Acad. Sci. USA 88: 8641-8645 (1991)], and, perhaps more importantly, because they share " β " signal-
20 transducing receptor components [Baumann, et al., J. Biol. Chem. 265:19853-19862 (1993); Davis, et al., Science 260: 1805-1808 (1993); Gearing et al., Science 255:1434-1437 (1992); Ip et al., Cell 69: 1121-1132 (1992); Stahl, et al., J. Biol. Chem. 268: 7628-7631 (1993); Stahl and Yancopoulos, Cell 74: 587-590 (1993)]. Receptor activation by this family of cytokines results from
25 either homo- or hetero-dimerization of these β components [Davis, et al., Science 260: 1805-1808 (1993); Murakami, et al., Science 260: 1808-1810 (1993); Stahl and Yancopoulos, Cell 74: 587-590 (1993)]. IL-6 receptor activation requires homodimerization of gp130. [Murakami, et al., Science 260: 1808-1810 (1993); Hibi, et al., Cell 63: 1149-1157 (1990)], a protein initially
3 identified as the IL-6 signal transducer [Hibi, et al., Cell 63: 1149-1157 (1990)]. CNTF, LIF and OSM receptor activation results from heterodimerization between gp130 and a second gp130-related protein known as LIFR β [Davis,